

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:  
GAL EHRLICH  
C/O ANTHONY CASTORINA  
2001 JEFFERSON DAVIS HIGHWAY  
SUITE 207  
ARLINGTON, VA 22202

**PCT**

REC'D 13 FEB 2006

WRITTEN OPINION

WIPO

PCT

(PCT Rule 66)

Applicant's or agent's file reference 01/22967		Date of Mailing (day/month/year) <b>08 FEB 2006</b> REPLY DUE within 1 months/days from the above date of mailing
International application No. PCT/IL01/01169	International filing date (day/month/year) 17 December 2001 (17.12.2001)	Priority date (day/month/year) 19 December 2000 (19.12.2000)
International Patent Classification (IPC) or both national classification and IPC IPC(7): A01N 63/00; A61K 48/00; C12N 5/00, 5/08, 15/63, 15/85 and US Cl.: 424/93.1, 93.21, 93.7; 435/455, 320.1, 325, 363, 366, 372		
Applicant INSIGHT STRATEGY AND MARKETING LTD.		

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.
2. This opinion contains indications relating to the following items:
  - I ☒ Basis of the opinion
  - II ☐ Priority
  - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - IV ☐ Lack of unity of invention
  - V ☒ Reasoned statement under Rule 66.2 (a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI ☐ Certain documents cited
  - VII ☐ Certain defects in the international application
  - VIII ☒ Certain observations on the international application
3. The applicant is hereby invited to reply to this opinion.
 

**When?** See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension. See rule 66.2(d).~~

**How?** By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

**Also** For an additional opportunity to submit amendments, see Rule 66.4.  
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.  
For an informal communication with the examiner, see Rule 66.6

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.
4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 19 April 2003 (19.04.2003)

Name and mailing address of the IPEA/US  
Mail Stop PCT, Attn: IPEA/ US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
Facsimile No. (571) 273-3201

Authorized officer  
*Quang Nguyen, Ph.D.*  
Telephone No. (571) 272-1600

WRITTEN OPINION

International application No.

PCT/IL01/01169

I. Basis of the opinion

1. With regard to the elements of the international application:\*

- ☒ the international application as originally filed
- ☒ the description:  
 pages 1-44, as originally filed  
 pages NONE, filed with the demand  
 pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the claims:  
 pages 45-60, as originally filed  
 pages NONE, as amended (together with any statement) under Article 19  
 pages NONE, filed with the demand  
 pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the drawings:  
 pages 1-4, as originally filed  
 pages NONE, filed with the demand  
 pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the sequence listing part of the description:  
 pages 1, as originally filed  
 pages NONE, filed with the demand  
 pages NONE, filed with the letter of \_\_\_\_\_

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.  
 These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

- ☒ contained in the international application in printed form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE \_\_\_\_\_
- ☐ the claims, Nos. NONE \_\_\_\_\_
- ☐ the drawings, sheets/fig NONE \_\_\_\_\_

5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."

WRITTEN OPINION

International application No.

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 29-132

because:

☐ the said international application, or the said claim Nos. \_\_\_\_\_ relate to the following subject matter which does not require international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 1-132.

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

**WRITTEN OPINION**International application No.  
PCT/IL01/01169**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

Novelty (N)	Claims <u>1-28</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>1-28</u>	YES
	Claims <u>NONE</u>	NO
Industrial Applicability (IA)	Claims <u>1-28</u>	YES
	Claims <u>NONE</u>	NO

**2. CITATIONS AND EXPLANATIONS**

Claims 1-28 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a stem cell preparation comprising stem cells carrying an exogenous extracellular matrix degrading enzyme, and a method of improving stem cells transplantation using the same.

**WRITTEN OPINION**

International application No.

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**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 1-28 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because of the claims are not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art for the following reasons.

The instant claims encompass a stem cell preparation comprising stem cells coated and/or transfected with any exogenous extracellular matrix degrading enzyme, and a method of improving stem cell transplantation using the same. However, apart from the disclosure that human blood cord stem cells coating with heparanase improve transplantation in the NOD-SCID mouse model as reflected by the % of cells in the mouse bone marrow that express human CD45 and/or CD15 compared with the uncoated human blood cord stem cells, the instant application fails to provide sufficient guidance for a skilled artisan on how to obtain similar results using a stem cell preparation coating with any other exogenous extracellular matrix degrading enzymes (e.g., collagenase, elastase, trypsin, pepsin, cathepsins). It is also unclear whether the same effects could be obtained using a stem cell preparation transfected with a nucleic acid encoding for any exogenous extracellular matrix degrading enzyme, particularly whether the expression of an exogenous extracellular matrix degrading enzyme has any effect on the viability, proliferation and/or differentiation potentials of the transfected stem cells, and therefore the desired end-results contemplated by Applicants. Physiological art is recognized to be unpredictable. Therefore, with the lack of sufficient guidance provided by the instant disclosure, it would have required undue experimentation for a skilled artisan to make and use the present broadly claimed invention.

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**Supplemental Box**  
(To be used when the space in any of the preceding boxes is not sufficient)

**TIME LIMIT:**

The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.